Docket No.: HOI-13202/16

AMENDMENTS TO THE CLAIMS

1-86 (Canceled)

87. (Previously presented) A method for assessing at least one quality parameter or at least one quantity parameter of a particle in a liquid material, said liquid material comprising particles having bound thereto or comprised therein at least one species of analytes in an amount of less than 1x10⁶ analyte detectable positions per particle.

comprising:

mixing the liquid material with at least one reagent material, said reagent material at least comprising a first targeting species capable of selectively and directly binding to an analyte position of said species of analytes said species of analytes having an amount of less than 1×10^6 analyte detectable positions and a labelling agent, wherein said labelling agent is a compound capable of emitting, absorbing, attenuating or scattering electromagnetic radiation to result in the generation of a detectable electromagnetic signal, wherein the first targeting species and the labelling agent are directly or indirectly coupled to each other,

arranging a volume comprising at least part of the mixture of the liquid material and the reagent material in a sample compartment having a wall part defining an exposing area, the wall part allowing electromagnetic signals from the volume in the compartment to pass through the wall to the exterior,

exposing, onto an array of active detection elements, a representation of electromagnetic signals originating from said labeling agent having passed through the wall part from the volume in the sample compartment, so that the ratio of a linear dimension of the image on the array of detection elements to the original linear dimension in the exposing domain is smaller than 20:1,

Docket No.: HOI-13202/16

detecting the representation as intensities by individual active detection elements,

processing the intensities in order to identify representations of electromagnetic signals from the particles as distinct from representations of electromagnetic signals from background, and

obtaining the at least one quality parameter or at least one quantity parameter from the result of the processing; wherein the sample is at a standstill during the exposure of the electromagnetic signals onto the array of active detection elements.

- 88. (Previously presented) The method according to claim 87, wherein the particle is selected from the group consisting of cells, cell walls, bacteria, plasmodia, virus, prions, fragments of cell walls, fragments of bacteria, fragments of plasmodia, fragments of virus, fragments of prions, clusters of cells, clusters of bacteria, clusters of plasmodia, clusters of prions, macromolecules and beads.
- 89. (Currently amended) The method according to claim 88, whereby wherein the particle is a bead, to which analytes are bound.
- 90. (Previously presented) The method according to claim 87, wherein the analyte is selected from the group consisting of proteins, polypeptides, peptides, lipids, carbohydrates, lipoproteins, carbohydrate-conjugated proteins, membrane constituents, receptors, genes, DNA, RNA, fragments of proteins, fragments of polypeptides, fragments of peptides, fragments of carbohydrate-conjugated proteins, fragments of membrane constituents, fragments of receptors, fragments of

Application No. 10/533,324 4 Docket No.: HOI-13202/16 Response to Notice of Non-Compliant Amendment

genes, fragments of DNA, fragments of RNA, clusters of proteins, clusters of polypeptides,

clusters of peptides, clusters of lipids, clusters of carbohydrates, clusters of lipoproteins, clusters

of carbohydrate-conjugated proteins, clusters of membrane constituents, clusters of receptors.

clusters of genes, clusters of DNA, clusters of RNA, and clusters of fragments.

91. (Currently amended) The method according to claim 88, whereby wherein the

analyte is bound to a cell membrane or cell nucleus membrane.

92. (Currently amended) The method according to claim 88, whereby wherein the

analyte is comprised in a cell.

93. (Currently amended) The method according to claim 92, whereby wherein the

analyte is comprised inside an organelle.

94. (Currently amended) The method according to claim 92, whereby wherein the

analyte is located on the surface of an organelle.

95. (Currently amended) The method according to claim 87, whereby wherein the

particles have bound thereto or comprised therein at least one species of analytes in an amount of

less than 5x105 analyte detectable positions.

96. (Currently amended) The method according to claim 87, whereby wherein the

particles have between 500 and 50,000 analyte detectable positions.

Application No. 10/533,324 5 Docket No.: HOI-13202/16 Response to Notice of Non-Compliant Amendment

97. (Previously presented) The method according to claim 87, wherein the particles

are cells selected from the group consisting of mammalian cells, insect cells, reptile cells, fish

cells, yeast cells, and fungi cells.

98. (Previously presented) The method according to claim 87, wherein the particles

are cells selected from the group consisting of blood cells, sperm cells, and bone marrow cells.

99. (Currently amended) The method according to claim 87, whereby wherein the

liquid material comprises at least two different species of particles.

100. (Currently amended) The method according to claim 99, whereby wherein only

one of the species of particles has bound thereto or comprised therein the species of analyte.

101. (Previously presented) The method according to claim 87, comprising binding at

least two distinct targeting species to at least two distinct species of analyte and labelling the at

least two distinct targeting species with two distinct labelling agents.

102. (Previously presented) The method according to claim 87, wherein one species of

analyte is selected from the group consisting of Cluster of Differentiation markers, Epithelial

Membrane Antigen, Estrogen receptor α, Cytokeratin Human, Cytokeratin 7, Cytokeratin 20,

Ki-67/PI, Phosphatidylserine, BCL2 Oncoprotein, soluble urokinase Plasminogen Activator

Application No. 10/533,324 Response to Notice of Non-Compliant Amendment

Docket No.: HOI-13202/16

Receptor, urokinase, a hormone bound to a receptor, a cell cycle related protein, a marker of

apoptosis, and Green fluorescent protein.

103. (Previously presented) The method according to claim 87, wherein one species of

analyte is selected from the group consisting of a chromosomal DNA sequence, a mitochondrial

DNA sequence, a chloroplast DNA sequence, a mRNA sequence, a rRNA sequence, a nucleotide

sequence comprising a single nucleotide polymorphism.

104. (Previously presented) The method according to claim 87, wherein one species of

analyte is a cell cycle related protein.

105. (Previously presented) The method according to claim 87, wherein the analyte is

a cell cycle related protein receptor.

106. (Previously presented) The method according to claim 87, wherein one species of

analyte is a marker of apoptosis.

107. (Currently amended) The method according to claim 87, whereby wherein the at

least one species of analyte is a medical marker of a disease.

108. (Currently amended) The method according to claim 87, whereby wherein the

reagent material comprises more than one first targeting species, each of said targeting species

being directed to a different analyte.

Application No. 10/533,324 7 Docket No.: HOI-13202/16
Response to Notice of Non-Compliant Amendment

109. (Currently amended) The method according to claim 87, whereby wherein the

targeting species is an antibody directed to the analyte species.

110. (Currently amended) The method according to claim 87, whereby wherein the

targeting species is a nucleotide probe complementary to a sequence of an analyte species.

111. (Previously presented) The method according to claim 87, wherein the targeting

species is an in situ hybridisation probe.

112. (Previously presented) The method according to claim 87, wherein the liquid

material is selected from the group consisting of body fluids, milk, milk products, waste water,

process water, drinking water, food, feed, mixtures of body fluids, mixtures of milk, mixtures of

milk products, mixtures of waste water, mixtures of process water, mixtures of drinking water,

mixtures of food, mixtures of feed, dilutions of body fluids, dilutions of milk, dilutions of milk

products, dilutions of waste water, dilutions of process water, dilutions of drinking water,

dilutions of food, dilutions of feed, extracts of body fluids, extracts of milk, extracts of milk

products, extracts of waste water, extracts of process water, extracts of drinking water, extracts

of food, and extracts of feed.

113. (Previously presented) The method according to claim 87, wherein the reagent

material is selected from the group consisting of fluorescently labelled antibodies, and antibodies

labelled with reactive molecules.

Application No. 10/533,324 8
Response to Notice of Non-Compliant Amendment

114. (Previously presented) The method according to claim 87, wherein the reagent

Docket No.; HOI-13202/16

material is selected from the group consisting of fluorescently labelled nucleotide probes, and

nucleotide probes labelled with reactive molecules.

115. (Previously presented) The method according to claim 87, wherein the reagent

material further comprises lysing agents and tissue fixative agents.

116. (Previously presented) The method according to claim 87, wherein the labeling

agent is selected from the group consisting of fluorescence quenching agents, light absorbing

agents, and fluorescence amplification agents.

117. (Currently amended) The method according to claim 87, whereby wherein the

labelling agent is selected from agents giving rise to one or several of the following phenomena:

attenuation of electromagnetic radiation, photoluminescence when illuminated with

electromagnetic radiation, scatter of electromagnetic radiation, raman scatter.

118. (Currently amended) The method according to claim 117, whereby wherein the

labelling agent is selected from the group consisting of fluorescein, phycoerythrin,

R-phycoerythrin, cyanine dves, acridine orange, thiazole orange, DAPI, propidium iodide,

ethidium iodide, 7-aminoactinomycin D, and Per CP.

Application No. 10/533,324 9 Docket No.: HOI-13202/16 Response to Notice of Non-Compliant Amendment

119. (Currently amended) The method according to claim 87, whereby wherein the

recording of image comprises the use of a confocal scanner.

120. (Currently amended) The method according to claim 87, whereby wherein the

image is recorded using an array of detection devices.

121. (Previously presented) The method according to claim 87, wherein the image is

recorded using a CCD, a CMOS, a video camera or a photon counting camera.

122. (Currently amended) The method according to claim 87, whereby wherein the

image is recorded so that the linear dimension of the image on the array of detection elements is

equal to the original linear dimension in the exposing domain.

123. (Currently amended) The method according to claim 87, whereby wherein the

enlargement ratio is below 10.

124. (Currently amended) The method according to claim 87 whereby wherein the

image is recorded in one exposure.

125. (Currently amended) The method according to claim 87 whereby wherein the

image is recorded in more than one exposure.

Response to Notice of Non-Compliant Amendment

126. (Previously presented) The method according to claim 125, wherein the

assessment of the number of particles is obtained on the basis of more than one image.

127. (Currently amended) The method according to claim 125, where wherein

information about the changes in the image in course of time is used in the assessment of the

number of particles.

128. (Currently amended) The method according to claim 87, whereby wherein a

distinction between at least two spectral properties of a labelling agent is used to obtain the at

least one quality parameter or at least one quantity parameter of the particles.

129. (Currently amended) The method according to claim 87, whereby wherein the

recording of an image further comprises exposing a first surface of the sample directly with

excitation light from a first light means having at least a first light source, by use of focusing

means detecting a fluorescence signal from the first surface of the sample onto a first detection

means comprising at least a first detector.

130. (Previously presented) The method according to claim 102, wherein the Cluster

of Differentiation marker is selected from the group consisting of CD3, CD4, CD8, CD16,

CD19, CD22, CD34, CD45, CD61, and CD91.

131. (Previously presented) The method according to claim 104, wherein the cell cycle related protein is selected from the group consisting of cycline, tumor suppresser protein.

Epidermal Growth Factor protein, Transforming Growth Factor beta, and Ki-67 protein.

132. (Previously presented) The method according to claim 131, wherein the cycline

protein is cyclin D1.

133. (Previously presented) The method according to claim 131, wherein the tumor

suppresser protein is p53 protein.

134. (Currently amended) The method according to claim 105, whereby wherein the

cell cycle related protein receptor is an Epidermal Growth Factor Receptor.

135. (Currently amended) The method according to claim 105, whereby wherein the

cell cycle related protein receptor is a Cyclin Dependent Kinase.

136. (Previously presented) The method according to claim 106, wherein the marker

of apoptosis is selected from the group consisting of membrane bound phosphatidylserines,

phosphatidylserines targeted with Annexin V, and BCL2 oncoprotein.

137. (Previously presented) The method according to claim 112, wherein the body

fluid is selected from the group consisting of blood, urine, saliva, bile, sperm, faeces, cerebro-

spinal fluid, nasal secrete, tears, and bone marrow.

138. (Previously presented) The method according to claim 116, wherein the fluorescence amplification agent is fluorescyl-tyramine or Cy3-tyramine.

12

- 139. (Previously presented) The method according to claim 118, wherein the cyanine dye is selected from the group consisting of Cy3, Cy5, Cy5.5, allophycocyanines, indotrimethinecyanines and indopentamethinecyanines.
- 140. (Currently amended) The method according to claim 87, whereby wherein the ratio of a linear dimension of the image on the array of detection elements to the original linear dimension in the exposing domain is equal to no more than 4.